Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims

Claim 1. (Withdrawn) A method of identifying a framework protein for subsequent engineering including the steps of: -

(i) creating a computer database which includes a plurality of entries, each said entry corresponding to a description of a location and orientation in 3D space of side chains of amino acid residues of a framework protein which compromises 70 amino acids or less and has 1-11 disulfide bonds, wherein the location and orientation of each side chain is simplified as a Cα-Cβ vector;

(ii) creating a query corresponding to a description of a location and orientation in 3D space of respective side chains of two or more amino acid residues of a sample protein which are required for a function of said sample protein, wherein the location and orientation of each side chain is simplified as a Cα-Cβ vector; and

(iii) searching said database with said query to thereby identify one or more hits wherein at least one of said hits corresponds to a respective said framework protein which has structural similarity to said sample protein.

Claim 2. (Canceled)

Claim 3. (Withdrawn) The method of claim 1, further including the step of modifying an amino acid sequence of said framework protein which corresponds to a hit, by substituting at least one amino acid residue of said sample protein to thereby create a modified framework protein.

Claim 4. (Withdrawn) The method of claim 3, wherein the at least one amino acid residue of said sample protein represents at a portion of at least one functional region of said sample protein.

Claims 5-15. (Canceled)

Claim 16. (Withdrawn) The method of Claim 1, wherein at step (iii) the hits are ranked according to structural similarity with said sample protein.

Claim 17. (Withdrawn) The method of Claim 1, wherein searching at step (iii) includes:

(a) identification of said hits by clique detection;

(b) filtering of said hits identified at step (a).

Claims 18-26. (Canceled)

Claim 27. (Currently Amended) A computer-readable medium encoded with a program for searching a protein database which comprises a plurality of entries, each said entry corresponding to a distance matrix representation of two or more $C_\alpha$- $C_\beta$ vectors of a framework protein, said program including the steps of:

(i) comparing a query with each said database entry, said query corresponding to a distance matrix representation of two or more $C_\alpha$- $C_\beta$ vectors; and

(ii) identifying hits by clique detection, wherein a hit is defined according to a minimum number of $C_\alpha$- $C_\beta$ vector matches that are determined by a comparison of unbinned distances between the distance matrix representation of said query and the distance matrix representation of each said entry; and

(iii) correlating at least one of said hits with a respective database entry to thereby identify a corresponding framework protein for subsequent modification to impart a desired property, characteristic or function to the framework protein.

Claim 28. (Currently Amended) A computer-readable medium encoded with a program ~~which filters said hits identified at step (ii)~~ for searching a protein database according to ~~of~~ claim 27, ~~by~~ wherein step (ii) of the program includes the additional step of:

(a) filtering said hits by comparing each said hit ~~of step (ii)~~ with said query to thereby select one or more of said hits having 3D structural similarity to said sample protein.

Claims 29-30. (Canceled)

Claim 31. (Currently Amended) A method of protein engineering including the steps of:-

(i) creating a computer database which includes a plurality of entries, each said entry corresponding to a description of a location and orientation in 3D space of side chains of amino acid residues of a framework protein which comprises 70 amino acids or less and has 1-11 disulfide bonds, wherein the location and orientation of each side chain is represented by a $C_\alpha$- $C_\beta$ vector;

(ii) creating a query corresponding to a description of a location and orientation in 3D space of each side chain[[s]] of two or more amino acid residues of a sample protein which are required for a function of said sample protein, wherein the location and orientation of each side chain is represented by a $C_\alpha$- $C_\beta$ vector;

(iii) searching said database with said query to thereby identify one or more hits wherein at least one of said hits corresponds to a respective said framework protein which has 3D structural similarity to said sample protein;

(iv) identifying the amino acid residue(s) of the framework protein hit identified at step (iii) that structurally correspond(s) to each of the two or more amino acid residues of said sample protein used to create the query at step (ii);

(v) determining which amino acid residue(s) identified at step (iv) is/are to be substituted by another amino acid to impart a particular property, characteristic or function to the framework protein identified as a hit; and

(vi) modifying said framework protein which corresponds to a hit, by substituting at least one amino acid residue thereof determined at step (v) with another amino acid to thereby create an engineered framework protein having the particular property, characteristic or function.

Claim 32. (Currently Amended) The method of Claim 31, wherein said another amino acid used for substitution at step (v) is at least one of the two or more amino acid residues used to create the query at step (ii).

Claim 33. (Previously Presented) The method of Claim 31 wherein the two or more amino acid residues of said sample protein used to create the query at step (ii) are non-contiguous in primary sequence.

Claim 34. (Previously Presented) The method of Claim 31, further including the step of determining that the engineered framework protein has greater stability than said sample protein.

Claim 35. (Currently Amended) The method of Claim 31, further including the step of determining that the engineered framework protein has increased structural similarity ~~compared to~~with said sample protein when compared to the structural similarity between said sample protein and said framework protein identified as a hit.

Claim 36. (Previously Presented) The method of Claim 31, further including the step of determining that the engineered framework protein exhibits a function which is either similar to, or inhibitory of, a function of said sample protein.

Claim 37. (Previously Presented) The method of Claim 31, wherein the sample protein is a cytokine.

Claim 38. (Previously Presented) The method of Claim 37, wherein the cytokine is selected from the group consisting of GH, IL-4, IL-6 and G-CSF.

Claim 39. (Withdrawn) The method of claim 1, wherein said query of step (ii) is a single query.

Claim 40. (Previously Presented) The method of Claim 31 wherein said query of step (ii) is a single query.

Claim 41. (Previously Presented) The method of Claim 31, wherein at step (v) at least one amino acid residue in addition to the amino acid residue(s) identified at step (iv) is identified for substitution by another amino acid to impart a particular property, characteristic or function to the framework protein identified as a hit.

Claim 42. (Previously Presented) The method of Claim 31 wherein the amino acids of the framework protein substituted at step (vi) are non-contiguous in primary sequence.

Claim 43. (Previously Presented) The method of Claim 31, wherein at step (iii) the hits are ranked according to structural similarity with said sample protein.

Claim 44. (Previously Presented) The method of Claim 31, wherein searching at step (iii) includes:

(a) identification of said hits by clique detection;

(b) filtering of said hits identified at step (a) by comparing each said hit with said query to thereby select one or more of said hits having 3D structural similarity to said sample protein.